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Indicators of Moisture and Ventilation System Contamination in U.S. Office Buildings as Risk Factors for Respiratory and Mucous Membrane Symptoms: Analyses of the EPA BASE Data

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We assessed associations between indicators for moisture in office buildings and weekly, building-related lower respiratory and mucous membrane symptoms in office workers, using the U.S. EPA BASE data, collected in a representative sample of 100 U.S. office buildings. We estimated the strength of associations between the symptom outcomes and moisture indicators in multivariate logistic regression models as odds ratios (ORs) and 95% confidence intervals (CI), controlling for potential confounding factors and adjusting for correlation among workers in buildings. This analysis identified associations between building-related symptoms and several indicators of moisture or contamination in office buildings. One set of models showed almost a tripling of weekly building-related lower respiratory symptoms in association with lack of cleaning of the drip pans under air-conditioning cooling coils (OR [CI] = 2.8 (1.2–6.5)). Other models found that lack of cleaning of either drip pans or cooling coils was associated with increased mucous membrane symptoms (OR [CI] = 1.4 (1.1–1.9)). Slightly increased symptoms were also associated with other moisture indicators, especially mucous membrane symptoms and past water damage to building mechanical rooms (OR [CI] = 1.3 (1.0–1.7)). Overall, these findings suggest that the presence of moisture or contamination in ventilation systems or occupied spaces in office buildings may have adverse respiratory or irritant effects on workers. The analysis, however, failed to confirm several risks identified in a previous study, such as condition of drain pans or outdoor air intakes, and other hypothesized moisture risks. Studies with more rigorous measurement of environmental risks and health outcomes will be necessary to define moisture-related risks in buildings.

Keywords indoor air quality, moisture, mold, symptoms, office building

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Episodes of nonspecific health complaints in indoor workplaces, not attributable to specific recognized disease or exposures, have been commonly reported in recent decades.(1) Sometimes referred to as sick building syndrome (SBS), these episodes have involved widespread complaints of symptoms and discomfort, including mucous membrane irritation, nasal symptoms, skin irritation, headache, fatigue, and breathing problems. Building occupants typically report that these symptoms occur while in the building and diminish when away from the building. The nonspecific symptoms involved in SBS have not been associated generally with objective findings on clinical examination or abnormalities in laboratory tests,(2) although recently developed objective tests for eye irritation and nasal patency show promise.(3)

Although specific causal exposures for SBS have not yet been consistently documented, research has identified a number of person-, job-, workplace-, and building-related risk factors for the same symptoms reported on survey questionnaires in noncomplaint buildings (e.g., presence of air-conditioning systems, low ventilation rate, high temperature, dust, endotoxin).(1,4,5) We refer to these symptoms as building-related symptoms (BRS). Research on BRS often has not considered lower respiratory symptoms (including wheeze, chest tightness, shortness of breath, and cough, sometimes

called asthma-like symptoms), which are the least commonly reported symptoms assessed in indoor environments.[6–8] However, these lower respiratory symptoms may, in some cases, indicate serious health effects, such as asthma, hypersensitivity pneumonitis, or humidifier fever.

A substantial body of research in residential environments has associated visible moisture and mold with upper and lower respiratory symptoms.[9–11] Empirical evidence has long suggested that moisture and related microbiological contamination in commercial and institutional buildings are related to occupant health complaints. Only recently, however, have studies reported the association of risks related to moisture and contamination in the buildings or ventilation systems of these nonindustrial indoor work environments with increased symptoms among workers.[6,8,12–14]

IEQ researchers have often hypothesized that surfaces within buildings or ventilation systems, when wet and dirty for extended periods, allow growth of microorganisms and releases into the indoor air that cause allergic, irritant, or toxic health effects, especially in susceptible groups. Less frequently scheduled or ineffective inspection, cleaning, and maintenance of ventilation systems often are assumed to allow more chronic accumulation of moisture and contamination on surfaces, leading to increased risk of microbiologic growth and subsequent harmful exposures to occupants. Whereas cleaning of occupied spaces may remove accumulated contamination, wet cleaning might increase risk of microbial growth and dissemination.

GOALS AND HYPOTHESES

The primary goals of this analysis were the following:

- To identify risk factors for building-related symptoms related to moisture, and contamination that may collect moisture (and support microbiologic growth), in buildings and ventilation systems in representative U.S. office buildings
- To replicate, in these representative buildings, previous findings from a set of U.S. office buildings investigated for indoor air quality complaints[12]

Our hypothesis is that certain features or practices in buildings, including those related to heating, ventilation, and air-conditioning (HVAC) systems and occupied spaces, increase the risk of moisture and contamination of potentially moist surfaces, which in turn increase the risk of exposure for occupants to microorganisms or other toxins that may have irritant, toxic, or allergic effects. Therefore, we predicted statistical associations between specific features or practices in buildings and lower respiratory and mucous membrane symptoms occurring among occupants in the buildings and improving when away from the building.

METHODS

We used the BASE data set, which was collected between 1994 and 1998 by the U.S. Environmental Protection Agency (USEPA) from 100 representative U.S. office buildings and includes a variety of information on both occupants and buildings. Descriptions of this study and the available data have been reported previously.[15,16] Briefly, the study selected a representative set of 100 office buildings from geographic regions throughout the United Sates, and then randomly selected within each building a study space with at least 50 occupants and no more than two air handling (ventilation) units. (Two study spaces included had three air handling units.) Data on demographics, work and workspace characteristics, symptoms, and health conditions were collected in questionnaires given to all occupants in each study space who were at work on Thursday and Friday of the chosen test week. Environmental data were collected by standardized inspections of the buildings and ventilation systems and environmental monitoring in the buildings. Facility managers were also interviewed and building plans reviewed. Each building was studied once, in either summer or winter, when either heating or cooling systems were most likely to be in use. The date of study was also recorded for consideration in analyses.

Outcomes used in analyses were "weekly, building-related" symptoms, defined as specific symptoms reported on the questionnaire to be experienced at least once per week within the last 4 weeks while at work and improving outside the building. We modeled risks for two symptom-based outcomes: lower respiratory symptoms (requiring at least one weekly building-related symptom from among wheezing, shortness of breath, chest tightness, and cough) and mucous membrane symptoms (requiring at least one weekly building-related symptom from among dry or itchy eyes, stuffy or runny nose, and sore or dry throat).

Independent variables used in these analyses included information from the self-completed occupant questionnaires (on demographic, health status, job, and workspace factors) and information collected by study personnel: inspection of ventilation systems, buildings, and occupied spaces; interviews with facility managers on building and ventilation system-related practices and history; and environmental monitoring for parameters such as temperature, relative humidity, and ventilation rate.

We selected from the BASE data an initial set of factors considered to indicate the presence of moisture, or contamination that might collect moisture, within the ventilation systems, buildings, or occupied spaces. These potential risk factors included the condition and scheduled maintenance of selected components in the ventilation system, current or past water damage at specific locations in the building, and frequency of wet cleaning in indoor spaces. We combined variables or category values in the original BASE data as necessary to create variables for analysis. When a study space had more than one associated air-handling unit, we assigned the "worst" condition or practice recorded for all associated air-handling units to the space as a whole. Because the variables for frequency of cleaning for drip pans and cooling coils were too highly correlated to include in the same model, we created

a summary variable, with the value for each study space set at the least frequent scheduled cleaning interval for either component. We also constructed additional multivariate models to estimate the risk for each of these two factors without the other.

We selected additional covariates for consideration as potential confounding variables or secondary risk factors, based on prior reported findings, theoretically plausible relationships, or crude associations with outcomes in BASE data. These covariates included personal variables related to demographic, health, and job factors (sex, age, education, job satisfaction, job demand, job conflict, asthma, mold allergy, hay fever, and years working in building). Models also included variables related to indoor conditions in the study buildings, based on environmental measurements: temperature (average number of hours multiplied by degrees per day that the indoor temperature was above 20°C),[17] relative humidity (mean indoor levels on 1 day), and ventilation rate (indicated by the mean difference in indoor/outdoor carbon dioxide concentrations, "delta CO_2," for each building).

We devised and followed a specific algorithm for selection and reduction of three subgroups of primary risk variables (HVAC condition and maintenance, moisture in the buildings or occupied spaces, and wet cleaning in the study spaces) and two subgroups of potential confounding variables (personal factors and measured indoor conditions) for initial inclusion in multivariate statistical models, before creation of more parsimonious models. Initial full models were then constructed of remaining variables from the five subgroup models and then further reduced based on contribution of terms to the model and confounding. Multivariate estimates were produced initially in multiple logistic regression models and finally in general estimating equation (GEE) logistic models adjusting for potential correlations among respondents within buildings. Details of the statistical modeling process are provided in the Appendix.

RESULTS

Data from 4326 BASE building occupants and study spaces within 100 buildings were available for analyses, although missing values on specific variables at either the individual or building level reduced numbers of observations in specific models. The number of workers occupying each study space during the week of BASE data collection ranged from 25 to 143, with a mean of 56. The mean response rate for the occupant questionnaire was 85%, ranging from 39% to 100% in individual buildings. The proportion of respondents with each of the weekly building-related symptom outcomes analyzed here was, for lower respiratory symptoms, 7.9% (9.0% of women, 1.8% of men), and for mucous membrane symptoms, 29.4% (34.2% of women, 19.6% of men).

The respondents to the occupant questionnaire have been described in detail elsewhere.[18,19] To summarize, 66% of respondents were female and 61% were between the ages of 30 and 49. Respondents' jobs, based on categories in the questionnaire, were 35% professionals, 34% clerical, 17% managers, and 14% technical. Approximately 18% of respondents had a high school diploma or less, 33% had completed some college, 36% had a college degree, and 18% had a graduate degree. Fifteen percent of respondents were current smokers. Respondents had worked in their buildings for an average of 5.9 years.

A complete description of the 100 BASE buildings is provided elsewhere.[19,20] Initial year of building construction ranged from 1850 to 1996, with 25 buildings built prior to 1951 and 22 after 1984. The average usable floor area of the buildings was approximately 16,000 m^2, ranging from 629 m^2 to 98,474 m^2, with 74% of buildings having 5000 m^2 or more in floor area. All but two of the BASE buildings had air-conditioning systems. Sixty-four buildings had no operable windows in the study space. The mean value of the indoor temperature metric used was 25 degree-hours above 20°C (equivalent to an average temperature of about 23°C over an 8-hour day), with a range of 2.2 to 42.8 degree-hours above 20°C. The mean relative humidity in the 100 base buildings was 38%, ranging from 8% to 66%. The mean delta CO_2 was 254 ppm, with a range from 40 to 608 ppm.

Table I lists the 16 risk factors for moisture or contamination, all dichotomous or categorical, included in initial models. Proportions of buildings at different levels of each risk variable are presented and correspond roughly to proportions for respondents. The list includes both the separate and combined variables for cleaning frequencies of drain pans and coils, although the separate variables were not included in the final models shown in the later table. Potential risk factors that were eliminated earlier in the analysis are listed in a footnote to Table I.

Bivariate Analyses

Table I also provides the unadjusted odds ratios (ORs) and 95% confidence intervals (CI) for each risk variable-outcome relationship assessed. Positive associations observed for weekly building-related lower respiratory symptoms and mucous membrane symptoms were generally similar in magnitude for infrequent scheduled cleaning of drain pans, infrequent scheduled cleaning of cooling coils, and the variable combining both; current water damage in study space, past water damage in basement, and past water damage from roof; and history of fire damage. Odds ratios for frequencies of cleaning did not increase monotonically as frequency decreased. Additionally, inverse associations for mucous membrane symptoms were observed with current or past water damage in study space mechanical room and less than daily wet floor mopping in the study space (the latter is equivalent to increased risk for more frequent floor mopping).

Results of Final Models

Table II presents results of the final models with the combined variable for frequency of pan and coil cleaning, after use of the reduction algorithm described in the Appendix, with multivariate adjusted ORs and 95% CIs from GEE models for

TABLE I. Unadjusted Odds Ratios and 95% Confidence Intervals for Associations Between Initial Risk Factors for Moisture and HVAC Contamination and Two Symptom Outcomes

Covariates	Percentage of Buildings (%)	Weekly Building-Related Symptom Outcomes: Lower Respiratory Symptoms OR (95% CI)		Mucous Membrane Symptoms OR (95% CI)	
HVAC Condition and Maintenance					
Drain pan cleaning frequency					
At least semiannually	19	1.0	—	1.0	—
At least annually	42	2.0*	1.4–3.0	1.4*	1.2–1.8
None	25	1.2	0.8–1.9	1.0	0.8–1.2
As needed	15	2.0*	1.3–3.0	1.5*	1.2–1.9
Cooling Coil Cleaning Frequency					
At least semiannually	13	1.0	—	1.0	—
At least annually	48	1.8*	1.2–2.8	1.4*	1.1–1.7
None	26	1.5	1.0–2.3	1.1	0.9–1.4
As needed	13	2.0*	1.2–3.1	1.5*	1.2–2.0
Pan and coil cleaning frequency					
At least semiannually	11	1.0	—	1.0	—
At least annually	40	1.8*	1.2–2.9	1.4*	1.1–1.7
None	19	1.7*	1.0–2.7	1.4*	1.1–1.8
As needed	30	1.3	0.8–2.1	1.0	0.8–1.2
Cooling Coil Condition					
Clean	50	1.0	—	1.0	—
Somewhat dirty	38	0.9	0.7–1.2	1.0	0.9–1.2
Very dirty	12	1.3	0.9–1.9	1.1	0.9–1.4
Moisture/Water Damage in Building or Occupied Space					
Current water damage					
Study space	14	1.3	0.9–1.7	1.2*	1.0–1.5
Mechanical room for study space	3	1.2	0.6–2.3	0.5*	0.3–0.8
Mechanical room in building	3	0.7	0.3–1.5	1.1	0.7–1.5
Basement	13	1.0	0.7–1.4	1.1	0.9–1.3
Roof	15	0.9	0.6–1.2	0.8	0.7–1.0
Past water damage					
Study space	32	0.8	0.6–1.0	0.9	0.8–1.0
Mechanical room for study space	4	1.0	0.5–1.7	0.6*	0.4–0.9
Mechanical room in building	17	1.0	0.7–1.4	1.1	0.9–1.3
Basement	28	1.3*	1.0–1.7	1.2*	1.0–1.4
Roof	50	1.3*	1.0–1.6	1.2*	1.1–1.4
History of fire damage in building	12	1.5*	1.1–2.0	1.3*	1.1–1.6
Wet Cleaning in Study Spaces					
Wet floor mopping frequency					
Daily	78	1.0	—	1.0	—
Less than daily	11	0.8	0.6–1.2	0.7*	0.5–0.8
As needed or none	11	1.2	0.9–1.7	1.0	0.8–1.3
Observations in Model		2888		2946	

Notes: Information from EPA BASE data collected in U.S. office buildings, 1994–1998. Potential risk factors eliminated early in the analysis based on inadequate variability or excess missing data include presence of air-conditioning system, presence of humidifiers and condition or maintenance of humidifiers, and presence of air-washing system. Potential risk factors eliminated due to excess collinearity or insufficient contribution in bivariate analyses include frequency of inspection of air handlers, coils, and drain pans; water damage variables collected at the building level about the study space while also collected for the study space level; water damage variables collected at the study space level about the building while also collected separately at the building level.

*p-value ≤ 0.05.

TABLE II. Multivariate Adjusted Odds Ratios and 95% Confidence Intervals for Associations Between Risk Factors for Moisture and HVAC Contamination and Two Symptom Outcomes

Covariates	Weekly Building-Related Symptom Outcomes: Lower Respiratory Symptoms OR (95% CI)		Mucous Membrane Symptoms OR (95% CI)	
HVAC Condition and Maintenance				
Pan and coil cleaning frequency				
At least semiannually	1.0	—	1.0	—
At least annually	1.5	1.0–2.5	1.3	1.0–1.6
None	1.6	0.9–2.7	1.4*	1.1–1.9
As needed	1.3	0.7–2.3	1.0	0.7–1.3
Cooling coil condition				
Clean	1.0	—	—	—
Somewhat dirty	0.8	0.5–1.1	—	—
Very dirty	1.1	0.8–1.5	—	—
Moisture/Water Damage in Building or Occupied Space				
Current water damage				
Study space	1.1	0.7–1.8	1.0	0.7–1.2
Mechanical room for study space	—	—	0.6*	0.5–0.9
Mechanical room in building	—	—	1.1	0.6–2.0
Basement	0.9	0.6–1.3	—	—
Roof	0.9	0.6–1.4	0.8	0.6–1.1
Past water damage				
Study space	0.9	0.6–1.4	1.1	0.9–1.4
Mechanical room for study space	—	—	—	—
Mechanical room in building	—	—	1.3*	1.0–1.7
Basement	1.3	0.9–1.7	1.0	0.9–1.2
Roof	1.1	0.9–1.5	1.1	0.9–1.3
History of fire damage in building	1.0	0.7–1.5	1.3	1.0–1.6
Wet Cleaning in Study Spaces				
Wet floor mopping frequency				
Daily	1.0	—	1.0	—
Less than daily	0.9	0.6–1.4	0.8	0.5–1.1
As needed or none	1.3	0.8–2.1	1.0	0.8–1.3

Notes: Information from final general estimating equation logistic regression models in the EPA BASE data collected from U.S. office buildings, 1994–1998. Each of the two final models contained terms for: (a) all risk factor covariates in Table II for which an estimate is shown; (b) ventilation rate and temperature; and (c) sex, education, job satisfaction, job demand, job conflict, asthma, mold allergy, hay fever, and years working in building. The lower respiratory symptom model also contained terms for age and current smoking. The mucous membrane symptom model contained terms for computer use, photocopier use, working more than 20 hours/week, and indoor relative humidity.
*p-value ≤ 0.05.

all the risk factors retained. Covariates in each final model are listed in the Notes for Table II.

In these models, there were no statistically significant elevations in risk for weekly building-related lower respiratory symptoms, but ORs were elevated for less frequent pan or coil cleaning and past water damage in basements. For weekly building-related mucous membrane symptoms, significantly elevated ORs were associated with less frequent pan or coil cleaning and past water damage in any building mechanical room. History of fire damage in the building was associated with marginally increased risk, and current water damage in the mechanical room of the study space was significantly protective.

In the multivariate models containing separate variables for the cleaning frequencies of drain pans and coils (not shown), strong associations were evident for less frequent cleaning of drain pans and building-related lower respiratory symptoms: ORs (95% CIs) were, for annual cleaning, 2.0 (1.0–3.9), and for no cleaning, 2.8 (1.2–6.5), relative to at least semiannual cleaning. Risks for cleaning of coils were only slightly elevated. Other estimates were similar to those in Table II.

DISCUSSION

It has not yet been possible to explain over 20 years' of symptom complaints from building occupants, as traditional industrial hygiene measurements generally have found no exposures above existing health standards. Studies associating symptoms with more general indoor environmental risk factors, presumably indicating unmeasured adverse exposures, have begun to point to certain classes of exposures—microbiologic and chemical—as the likely culprits. One hypothesized cause, increasingly plausible based on mounting evidence, is the presence of moisture on surfaces in the buildings or ventilation systems, leading to increased risk of microbiologic growth and subsequent harmful exposures to occupants, especially in the presence of accumulated particles or dust that hold moisture and also provide nutrients for microorganisms.

As expected, infrequent cleaning of drip pans or cooling coils was associated with increased ORs for both lower respiratory and mucous membrane symptoms. This risk was especially large for drain pans that were never cleaned—almost a tripling of risk in one model for lower respiratory symptoms—although the correlation between cleaning frequencies of drain pans and cooling coils prevented simultaneous estimation of the two risks. Past water damage, either in basement or building mechanical rooms, and history of fire damage in buildings were associated with some increased risk of symptoms.

Contrary to expectation, however, most other water damage variables were not substantially associated with symptoms, and current water damage in the study space mechanical room was associated with a substantial *reduction* in mucous membrane symptoms. This latter reduction and the absence of association for several other water damage variables may have been due to the rarity (only 3 or 4 out of 100 buildings) of several water damage conditions, leading to inaccurate risk estimation. More of the expected associations for water damage (e.g., current water damage in study space, basement, and roof, and history of fire damage) were seen in unadjusted models but not in adjusted models, presumably due to strong intercorrelations. The analysis also unexpectedly failed to find associations between symptoms and other indicators of moisture and contamination that are strongly suspected of leading to respiratory or mucous membrane health effects, for instance, cleanliness (as opposed to maintenance frequency) of drip pan, cooling coil, or outdoor air intake.[8,12]

The EPA BASE data provide the opportunity for the first broad, nationwide assessment in a representative set of U.S. buildings of the associations between suspected indoor environmental risk factors and nonspecific symptoms in office workers. The findings in this analysis of the BASE data related to moisture and presumed resulting microbial contamination are not consistently supportive of prior findings or hypothesized relationships. Findings agreed with expectations only for a small number of hypothesized relationships.

Findings Compared with Prior Research, Theory, or Experience

Prior analyses of the BASE data have shown associations between lower ventilation rates in the BASE buildings and increases in several building-related symptoms, both in a 40-building subset[21] and in the full set of 100 buildings.[22] These prior findings tend to corroborate the presence of indoor air contaminants, *removable* by ventilation, that cause building-related symptoms. Yet the current analyses identified few of the expected sources of these contaminants as risks.

A large body of research has documented associations between evident moisture or mold in residences and respiratory health effects.[9] Some recent research has found relations between health effects and specific measurements of culturable microorganisms in dust or air. In offices and other nonindustrial indoor workplaces, less research has been reported on these relationships. Mendell et al.[7] found frequent, building-related lower respiratory symptoms in California office workers to be associated with presence of air conditioning, relative to naturally ventilated buildings. Reviews show that many other studies repeating this comparison in many countries have confirmed the consistency of this relationship.[1,23] A common explanation of these findings is that poorly maintained or operated ventilation systems may produce and disseminate contaminants that lead to increased symptoms among building occupants.

One of the few prior studies on moisture or contaminants in offices and related health risks was a 1992–1993 National Institute for Occupational Safety and Health (NIOSH) study of buildings requesting investigation because of poor IEQ. Two published papers reported analyses of the associations in that study between indicators of moisture and contamination and symptoms among building occupants.[8,12] In partially adjusted models, each containing one environmental risk factor adjusted for personal factors, both papers reported that increased lower respiratory symptoms were associated with many aspects of the design and maintenance of HVAC systems and buildings. Identified risk factors included air intakes near standing water, debris inside air intake, poor pan drainage, dirty ductwork, dirty filters, and general presence of moisture or lack of cleanliness in HVAC systems; protective factors included daily vacuuming. The later publication[12] on these data also included a full multivariate analysis that simultaneously considered the multiple environmental risk factors related to moisture in the office buildings. Significant environmental risk factors identified in multivariate models included debris in air intakes, poor pan drainage, and water damage in occupied spaces.

Park et al.[24] found that a semiquantitative mold exposure index based on extent of water stains, visible mold, mold odor, or moisture in office buildings was associated with increased risk of lower and upper respiratory symptoms. Wan and Li[25] found that symptoms of eye irritation, cough, and lethargy increased with the number of moisture-related factors present in Taiwanese office buildings.

Limitations of Study and Analyses

The BASE data, although the largest and most comprehensive collection of standardized data from representative office buildings in the United States, have many inherent limitations for epidemiologic analyses. For instance, the subjective, self-reported health outcome assessments used are imprecise metrics of underlying biologic processes and are possibly biased in some buildings due to concerns of occupants or other factors. Furthermore, the wide variation among BASE buildings in response rate to the occupant questionnaire (an overall mean of 85%, a minimum of 35%) allows for substantial bias of symptom reporting in low-response buildings if responders differed from the target population. At the time BASE was designed, questionnaire assessments of health outcomes were the only apparently feasible method to use, given the issues of cost, the difficulties in obtaining permission to conduct research on human subjects, and the challenges more clinical measures posed for securing participation by building owners, managers, and occupants. Only more recently have more objective health outcome measurements been used successfully in studies of moisture in buildings, for example, Walinder et al.[26] and Taskinen et al.[27] However, Cox-Ganser has recently shown that in a heavily moisture-damaged complaint building with documented building-related respiratory illness, 38% of those with symptoms had abnormal lung function or used asthma medication versus 11% of those without symptoms.[28]

The metrics used for categorizing conditions of cleanliness and moisture of ventilation systems and spaces, based on inspections and questionnaires using imprecise, nonquantitative, and nonstandardized categories, can be subject to substantial error. Reports from inspections are based on subjective assessments. The responses of facility personnel regarding the frequency of their inspections and maintenance activities are subject to recall bias and self-protective misreporting. Even highly standardized and accurate reporting based on visual inspection may correlate only roughly with underlying causal exposures. The inevitable random misclassification from errors both in the primary risk factors and outcomes, all subjectively assessed, could have resulted in bias toward the null and obscured true associations.

Furthermore, risk factors such as dirty or infrequently cleaned drain pans may simply be proxies for general low standards of maintenance rather than directly representing moisture and microbial risks. More standardized and exact methods of assessing water damage, such as the semiquantitative mold exposure index recently reported by Park et al.[13] would be preferable, until actual causal exposures are identified and appropriate measurement tools developed.

The many environmental factors initially assessed in this analysis were often so intercorrelated that some could not be included in the same models with others. Some risk factors of interest, such as humidification, and several water damage variables could not easily be assessed because of inadequate variability among buildings or excess missing data. Limited variablility among factors included in the analysis may have led to spurious findings, such as the protective association found for current water damage in the mechanical room for the study space.

It is possible that subjectively assessed factors not showing increased risk within the range occurring in the BASE "normal" buildings would be associated with risks within the NIOSH population of buildings with health complaints, because truly adverse levels of the environmental conditions of interest (e.g., more substantial moisture and contamination of ventilation systems) are present in only a small proportion of the normal building population. In addition, buildings with well-publicized histories of health-related investigations were excluded from BASE. Thus, the range of conditions in the BASE buildings included in this analysis may not have included enough very badly designed, maintained, or contaminated buildings to allow *detection* of associations. The NIOSH study, on the other hand, was conducted entirely in buildings being investigated for indoor air quality complaints, and thus may have included more buildings at the higher levels of the risk factors.[12]

It is possible that some BASE buildings were subjected to special cleaning before the scheduled arrival of BASE study personnel, although no evidence is available to suggest this. Such action would, without influencing health effects during the previous 4 weeks referenced in the symptom questions, move a building incorrectly into the "clean" categories for conditions of specific components studied. The same would be true for buildings where facility managers exaggerated the frequencies of cleaning or inspection reported to study personnel in interviews. This misclassification would tend to bias any actual associations toward the null, obscuring any true association. The possible occurrence of such actions could help explain the lack of some expected findings.

Despite the large size of this study, the environmental variables were collected in only 100 buildings, which allowed limited analysis of variation in these factors. The analysis was carried out at the respondent level despite environmental data collection at the building level. Correlations of responses among occupants of each building may sometimes produce spuriously inflated precision, leading to erroneously narrow confidence limits on estimates. Final estimates from GEE models, however, adjusted for this and found essentially no effect of correlated occupants in the simpler logistic models.

The difference between an estimated OR and 1.0 approximates the proportional increase or decrease in symptom prevalence, when overall prevalence of a symptom is less than approximately 20%. For example, an OR of 1.3 indicates an approximate 30% increase in prevalence. Prevalence of lower respiratory symptoms was less than 8%; however, prevalence of mucous membrane symptoms was approximately 29%, so ORs for this outcome will slightly overestimate the true proportional change in prevalence.

This analysis included a large number of initial risk factors and over 35 statistical tests. Chance would predict p-values less than 0.05 for approximately two of these tests even

in the absence of true associations. Thus, some of the few associations found and reported here may have occurred without true underlying associations. Replication of these findings will be necessary.

CONCLUSIONS

This analysis found, in one set of models, an approximate doubling or tripling of frequent building-related lower respiratory symptoms in association with infrequent or no cleaning of air-conditioning drip pans. Other models found infrequent cleaning of either drip pans or cooling coils was associated with 30–60% increases in both lower respiratory and mucous membrane symptoms. Increased risk for symptoms also was associated with other moisture factors, especially mucus membrane symptoms and past water damage to mechanical rooms.

These findings, from a representative set of U.S. office buildings, should be reasonably generalizable to the large number of similar office buildings throughout the United States.[20] Even given the generally moderate increases in risk found, if the associations were causal, it would suggest an important but preventable increase in symptoms among the very large proportion of the U.S. work force employed in indoor environments. Increased symptoms at work are likely to diminish both the well-being and work performance of the office workers. The larger clinical significance of these increased symptoms is unknown, but microbiologic exposures in some cases can cause sensitization and chronic illness.

RECOMMENDATIONS

These findings, although not fully consistent with prior studies, suggest that frequent cleaning of air-conditioning drain pans and coils, and general prevention and mitigation of other water incursions into buildings and HVAC systems, is advisable for prevention of building-related symptoms. These actions also should be considered in remediation efforts for complaint buildings. Finally, further research is necessary to define the scale and nature of these effects and document effective preventive measures.

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APPENDIX—DETAILS OF CONSTRUCTION AND REDUCTION OF STATISTICAL MODELS

All analyses were conducted using SAS (Version 8.2, SAS Institute Inc.). In short, we constructed multivariate logistic regression models (Proc Logistic). Then, because of potential correlation between individuals within the study buildings, we transferred terms in each final model to a logistic model with Generalized Estimating Equations (GEE, with exchangeable correlation matrix, using Proc Genmod).

We first selected covariate variables for initial use in analyses, using the following steps:

- Based on initial univariate analyses of primary risk factors and other covariates, we excluded from analyses variables with inadequate variation among buildings or respondents, or excess missing values (see Table I).
- Based on bivariate (unadjusted) analyses of the remaining covariates with the two outcomes, we collapsed value categories for some variables that had very small groups or adjacent groups with similar levels of risk, and excluded covariates with p-values larger than 0.25 for association with both outcomes.
- To reduce the large number of potentially relevant independent variables, we further omitted or combined selected covariates or collapsed value categories where appropriate, based on collinearity and crude associations assessed in cross-tabulations, bivariate analyses, and initial small logistic regression models for each outcome containing subsets of potentially correlated covariates (see Table I).

With the resulting reduced set of covariates, we constructed five initial subgroup models, identical for each outcome, containing independent variables of the following types: HVAC conditions and maintenance, moisture in the buildings or occupied spaces, wet cleaning practices in the study spaces, building ventilation rate and thermal factors, and personal factors. The first three subgroups contained primary risk factors for this analysis (listed in Table I); the latter two contained other potential risks or confounders (listed in text). Separately for each primary symptom outcome, we reduced these subgroup models (eight in all, excluding the two models for wet cleaning, each containing only one covariate). We used the following algorithm: sequentially removing covariate terms with the largest p-values exceeding 0.25, retaining all those for which p did not exceed 0.25.

For each outcome, we then used all covariates remaining in the five subgroup models to construct the initial full models for the outcome, and reduced this initial model using a SAS macro (written by co-author QL) to perform the following steps:

- Sequentially removing the covariate term with the largest p-value exceeding 0.25, until p-values for all remaining terms did not exceed 0.25, with these exceptions:
    - all initially present primary risk factors were forced to remain
    - variables with *a priori* status as key confounding or risk factors were forced to remain (e.g., sex, ventilation rate, temperature)
    - any covariate whose removal changed the estimate for any primary risk term by over 10% was considered a confounder and retained
- If goodness-of-fit for a final reduced model was considered inadequate (Hosmer and Lemeshow Goodness-of-Fit Test p-value less than 0.20), increasing the threshold p-value for retaining terms in the model iteratively by 0.05 until achieving an adequate fit.
- Refitting the final model using GEE with SAS Proc Genmod (Table II).